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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: **Docket No. 2005D-0348**
Comments on Draft Guidance for Industry and FDA Staff: Procedures for Handling Post-Approval Studies Imposed by PMA Order

To Whom It May Concern:

These comments are filed on behalf of the Cook Group, Inc. ("Cook"), a holding company of international corporations engaged in the manufacture of diagnostic and interventional products for radiology, cardiology, urology, gynecology, gastroenterology, wound care, emergency medicine, and surgery. Cook pioneered the development of products used in the Seldinger technique of angiography and in techniques for interventional radiology and cardiology. Cook products benefit patients by providing doctors with a means of diagnosis and intervention using minimally invasive techniques, as well as by providing innovative products for surgical applications. Cook sells over 15,000 different products which can be purchased in over 60,000 combinations.

The Cook Group respectfully submits these comments on the draft guidance entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order " (the "Guidance"), issued September 15, 2005 by the Food and Drug Administration ("FDA"), Center for Devices and Radiological Health ("CDRH"), Division of Postmarket Surveillance, Office of Surveillance and Biometrics.

We commend the FDA for issuing this guidance. Not only is direction regarding the specific information FDA wants in a post-market report helpful, but obtaining such information will contribute to assuring the agency and sponsors that useful data will likely result from post-market studies. As such, the guidance provides additional support for FDA's reliance on such studies to answer some pre-market questions, thus, ensuring least burdensome and more timely review decisions.

Following introduction of novel technologies to the marketplace, Cook has often conducted post-market surveillance. Sometimes such surveillance has been mandated by FDA as a condition of approval. In other instances, it has been initiated at Cook's discretion, in the interest of evaluating issues of interest that are unnecessary to an approval or clearance decision, yet important enough to explore and address. Additionally, the longer term follow-up of post-market studies provides a good opportunity to identify use considerations that shorter term studies may not reveal, thus, increasing our vision for next generation devices. It is from this perspective that we offer our comments.

To begin, we would like to raise some large, overarching issues where FDA assistance and guidance are sorely needed. The terms post-market studies and post-market surveillance can mean many different things, including clinical studies, many types of registries, and "other investigations" as noted in the draft guidance. They can involve a few or scores of institutions.

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There is significant confusion as to when informed consent and IRB approval are necessary for the various studies. It would be most helpful if FDA would clearly define what requirements apply for the benefit of both IRBs and manufacturers so that studies can be carried out effectively and efficiently.

Further, while we believe it is clear that HIPAA regulations authorize health care providers to give medical device manufacturers protected health information for post-market clinical follow-up related to their products, neither the HIPAA nor FDA regulations require or promote the release of this information to manufacturers, unless the information relates to a reportable adverse event. Therefore, although manufacturers are required to provide post-market clinical follow-up to multiple regulatory agencies and manufacturers, being liable for product safety, desire to know the safety profile of their products, access to this valuable safety information is restricted by current implementations of the regulations. We believe it is very important that FDA find an effective way to communicate to relevant institutions the lawfulness and the necessity to provide such information to manufacturers in order to facilitate complete and meaningful post-market reports to the agency.

We would also like to make some very specific suggestions to improve the guidance. These suggestions are as follows:

a) The guidance provides a list of information recommended to be included in periodic reports to the agency. (Page 10). This list raises several questions and is likely to cause confusion. The information requested is not unreasonable, but it appears to us that some thought should be given as to which elements are needed for the various types of reports mentioned in the guidance. We believe it is important to be very specific about what information is requested.

   For example, the list includes the purpose of the study and the patient selection information. This information is basic to the protocol. Would submission of the protocol with each report satisfy the agency request? If so, it would be clearer to simply request the protocol. If the guidance is asking for only part of the protocol, such as the purpose/objectives section and the inclusion/exclusion criteria, it would be helpful to specifically request that information. If the agency wants only an abstract of the protocol, the level of detail will vary substantially unless more specific guidance is provided. FDA should clearly address these issues now rather than through numerous deficiency letters to manufacturers. The clarification would benefit both FDA reviewers and manufacturers, saving time and resources for both.

   The requirement for substantial information relating to the schedule seems appropriate only if there are unexpected, significant changes to the schedule. Otherwise, this information would seem to be burdensome, in that it requires a reanalysis of planning with respect to each item listed for each report.

b) The guidance could be interpreted to require a summary of data and interpretation of results for each report. This would constitute an interim analysis which has significant statistical implications and would affect sample size calculations and the statistical analysis plan, and may invalidate some blinded study designs.

Should the guidance be interpreted to require all post-market study designs to plan for interim analyses every six months? How is study bias minimized with so many interim analyses of blinded data? Further clarification is needed as to the type of information required. We believe it is possible for FDA to adequately monitor the progress of post-market clinical follow-up activities without requiring interim analyses, which may adversely affect study design and statistical validity.

c) Clarification and consistency of defined terms would be helpful.

The guidance defines "Post-Approval Study," (Page 6), yet in other places the document utilizes the term "post-market study." Is there a distinction between post-approval and post-market studies? If not, consistency would be helpful.

The guidance includes the term "Post-Approval Study Protocol." (Page 7). It would be helpful to include it in the definitions rather than in text since there is a definition section.

d) The guidance requests the contact information for the PMA holder and the contact information for the submission correspondent (if different from the PMA holder). (Page 8). Further in the same list is additional contact information. (Page 9, immediately preceding Section II). Whose contact information is this?

e) The guidance requires interim study status reports at six-month intervals. It is unclear, however, whether these reports are due at the six-month anniversary dates or are intended to contain activity throughout the six-month period and therefore are to be submitted shortly after the end of the six-month period. It would be helpful to clarify this issue.

f) The guidance refers to a "Final Post-Approval Study Report". If a study report is submitted to FDA and FDA intends to point out deficiencies requiring revision of the study report, it is unclear whether the initial submission should be considered a "Draft Final Post-Approval Study Report" or the revised submission should be considered a "Revised Final Post-Approval Study Report". It would be helpful to clarify this issue.

Cook supports FDA's effort to provide guidance on the format, content, timing and review of reports on post-approval studies imposed by PMA order. We appreciate the opportunity to share our comments and look forward to the issuance of the guidance in final form. We would also be extremely grateful for assistance in clarifying the regulatory issues we mentioned above so that companies such as ours can effectively carry out post-market surveillance.

Respectfully,

Neal E. Fearnot

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